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REMARKS

Comments About Amendments Made

Claims 3, 9, 10 and 19-21 have been amended to address the examiner's objections to the claims. Claims 26 and 27 have been amended to correct a typographical error and represents a narrowed embodiment of claim 25. It is believed that no new matter has been added and that entry of the amendment would simplify matters for Appeal.

35 U.S.C. 112, first paragraph rejection (scope of enablement)

The applicants agree with the examiner's recitation from MPEP 2164.05. However, the applicants disagree with the examiner's apparent assertion that "a reasonable basis to question enablement" has been established. Again, the applicants refer back to the *Wands* factors and MPEP 2164.01(a) – "There are many factor to be considered when determining whether ***there is sufficient evidence*** to support a determination that a disclosure does not satisfy the enablement requirement...It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider ***all the evidence*** related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole."

Not only has certain factors not been considered, there is no evidence to form the "reasonable basis to question enablement". The evidence provided thus far are mere conclusionary statements offered by the examiner with no basis or grounding in fact(s).

For completeness, the full response from the 30 September 2002 filing is reproduced below:

Claims 1, 2, 4-8 and 11-15 were rejected by the examiner as being non-enabling for the treatment of rosacea and coperose. In response to the applicants' previous arguments, the examiner responded that "...the Applicant has to submit *an evidence* that the NO-synthase inhibitors are, in fact, effective in preventing rosacea and couperose.".

However, based upon the examiner's development of her non-enablement rejection based upon her *Wands*-type analysis (see MPEP 2164.01(a)), there does not appear to a basis for a requirement for a submission of "evidence". It is noted that not only does the MPEP not require that "evidence" be present in the specification, in certain instances it is not even necessary for the subject matter of the claimed invention to be recited in the specification if the subject matter was present in the claim as originally filed and the limitation in and of itself may enable one skilled in the art to make and use the claim containing

the limitation (see last paragraph of MPEP 2164).

MPEP 2164.01 (Test of Enablement), in addition to defining the standards upon which enablement is to be based (see *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), also states that "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patient coupled with information known in the art without undue experimentation.' A patent need not teach, and preferably omits, what is well known in the art.(citations omitted)"

Most importantly, MPEP 2164.01 also teaches that "Determining enablement is a question of law ***based on underlying factual findings*** (bold and italics added by author). *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

The examiner's original lack of enablement rejection as it was presumed to apply to the undue experimentation factors from MPEP 2164.01(a) is listed below (examiner's comments in bold and quotation marks):

Factor	Examiner's statement
(A) The breadth of the claims;	**Not addressed**
(B) The nature of the invention;	**"The burden of enabling the prophylaxis or prevention of a disease (i.e. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those humans susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition."**
(C) The state of the prior art;	**Not addressed**
(D) The level of one of ordinary skill in the art;	**Not addressed**
(E) The level of predictability in the art;	**Not addressed**
(F) The amount of direction	**"Further, the specification does not provide guidance**

provided by the inventor;	**as t how one skilled in the art w uld go ab ut screening those patients susceptible to rosacea and couperose."**
(G) The existence of working examples; and	**Not addressed**
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.	**"Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention."**

As can be seen from the chart above, only three of the eight undue experimentation factors have been addressed. Furthermore, even with the three factors which have been addressed, each appear to be pronouncements made by the examiner, i.e. there is no indication that the statements made were based upon "underlying factual findings". The requirement for factual findings is even more relevant in the present case as it has previously been held that there is enablement for the treatment of rosacea and couperose ***and*** the specification indicates that patients previously afflicted with rosacea and/or cuperose do not have a recurrence of the condition(s) when treatment is continued (i.e. was prevented), see page 6, second to last paragraph of specification.

Although the examiner would be justified in rescinding this rejection based upon the above arguments, if this is the only issue remaining which prevents an allowance of the pending claims, in order to expedite prosecution of the application, the examiner may delete reference to prophylaxis in an examiner's amendment; the applicants' reserve the right to resubmit the broader claim as part of a divisional application.

35 U.S.C. 102(b) rejection

Claims 1-4, 7, 8, 11, 14, 15 and 18 remain rejected by the examiner as being anticipated by Giacomoni (WO 96/26711 – English language translation previously provided by applicants).

The only rebuttal provided by the examiner to the arguments presented against the Giacomoni reference

is reproduced below:

"With respect to the 102 rejecti n over the Giacomoni reference, the Applicant argues that Giacomoni fails to anticipate the instant claims, it is noted that Giacomoni explicitly teach treating rosaceous acne with compositions containing a NO-synthase inhibitor in combination with a retinoid. Further, the effective amount of NO-synthase inhibitors in the compositions of Giacomoni overlaps with that of the instant invention. See claim 2 of the translation and p.7 of the instant specification."

However, the passages from Giacomoni corresponding to the examiner's statements made above (claim 2 and the last 7 lines of page 7 of the English translation of WO 96/26711) are mere "invitations to experiment". There is no positive recitation from Giacomoni that a composition containing an NO-synthase inhibitor can be used to treat rosacea or couperose as claimed by the applicants.

Giacomoni merely states "ideal for use in the following areas of treatment" (what does this mean? That it is an active ingredient? That it can be used as an additive for other compositions?) and further suggests that "treatment" is intended to include compositions which contain retinoids. Moreover, even the passage which recites "rosaceous acne". Claim 2 of Giacomoni is a "use" claim and as best as it can be translated into a corresponding method of using or composition claim, it is directed toward reducing the skin irritation effect of "products applied topically in the cosmetic or pharmaceutical field", not towards an effective amount of an NO-synthase inhibitor for treating rosacea or couperose.

As stated previously, MPEP 2131 states that to anticipate a claim, the reference must teach every element of the claim and quotes from *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d, 1913, 1920 (Fed. Cir. 1989) which states "***The identical invention must be shown in as complete detail as is contained in the...claim.***" The Giacomoni reference does not meet this standard.

35 U.S.C. 102(e) rejection

Claims 3, 9, 19 and 19-27 remain rejected by the examiner as being anticipated by Breton et al. (U.S. Patent 5,795,574).

Similar to the Giacomoni reference, the Breton et al. reference fails the "complete detail as is contained in the claim"-test. The various passages cited by the examiner appear to highlight the importance of substance P and an extract of a non-photosynthetic filamentous bacterium in the Breton et al. reference and forces one of ordinary skill in the art to engage in picking and choosing through the laundry list of

the claim"-test. The various passages cited by the examiner appear to highlight the importance of substance P and an extract of a non-photosynthetic filamentous bacterium in the Breton et al. reference and forces one of ordinary skill in the art to engage in picking and choosing through the laundry list of options listed in the Breton et al. specification. It is unclear one of ordinary skill in the art would ever be directed to the applicants' composition or method of treating rosacea or couperose through use of a NO-synthase inhibitor merely from the specification and claims of Breton et al.

35 U.S.C. 103(a) rejection

Claims 5, 6, 12 and 13 remain rejected by the examiner as being obvious over Giacomoni, *ibid.*, in view of Breton et al., *ibid.* or Ptchelintsev et al. (U.S. Patent 5,847,003).

The Breton et al. and Ptchelintsev et al. references were first relied upon by the examiner in the office action of 12 October 2000 to account for the differences with respect to the UVA and/or UVB filters described in the applicants' claims 5, 6, 12 and 13. As this rejection is contingent upon Giacomoni being a viable reference to support the rejection, the applicants' hold that the response made above in the 102(b) response also applies with respect to establishing that Giacomoni does not render the applicants' invention obvious even in light of Breton et al. and Ptchelintsev et al.

Even if *in arguendo* the rejection of the claims cited in the 102(b) rejection were upheld (or upheld as part of a 103(a) rejection), there is no teaching or suggestion to make the appropriate substitution from Breton et al. and/or Ptchelintsev et al. and selectively substitute it into the teaching of Giacomoni nor is there any suggestion that one could selectively "pick and choose" only one element within the context of Breton et al. and/or Ptchelintsev et al. inventions and substitute it into the context of the teaching of Giacomoni. (It has been held that "...'***Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention.***' see *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998).

As the motivation appears for making the combination appears to be based on an assertion of implicit motivation rather than specific teaching (express showing) from any of the three references cited, the examiner is reminded that whether the USPTO relies on an express or an implicit show of motivation, ***it must provide particular findings related to its conclusions, and the showing must be clear and particular.*** Broad conclusionary statements standing alone are not "evidence". see *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999).

Closing

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the foregoing Amendment under 37 CFR § 1.116 (10 pages total) is being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below:

Date: **20 February 2003**

By: Vilma I. Fernandez

COPY OF CLAIMS SHOWING AMENDMENTS MADE

3. Cosmetic or dermatological topical preparations comprising a NO-synthase inhibitor or salt thereof which is selected from the group consisting of **[L-MEA]** ***N^G-monoethyl-L-arginine monoacetate***, 2-Iminobiotin, **[L-NIO]** ***L-N^5-(1-iminoethyl)-ornithine***, S-Methylisothiourea sulphate, S-Methyl-L-thiocitrulline, **[L-NIL]** ***L-N^G-(1-iminoethyl)lysine***, 7-Nitroindazole, **[PBITU]** ***S,S'-1,3-Phenylene-bis(1,2-ethanediyl)-bis-isothiourea***, L-Thiocitrulline, **[alpha-N-acetyl-L-NAME]** ***alpha-N-acetyl-N^G-nitro-L-arginine methyl ester*** and salts thereof.

9. Cosmetic or dermatological topical preparations according to Claim 3, wherein said NO-synthase inhibitor or salts thereof is selected from the group consisting of 2-Iminobiotin, **[L-NIO]** ***L-N^5-(1-iminoethyl)-ornithine***, S-Methylisothiourea sulphate, S-Methyl-L-thiocitrulline, **[L-NIL]** ***L-N^G-(1-iminoethyl)lysine***, 7-Nitroindazole, **[PBITU]** ***S,S'-1,3-Phenylene-bis(1,2-ethanediyl)-bis-isothiourea***, L-Thiocitrulline, and salts thereof.

10. Preparation according to Claim 9, wherein said NO-synthase inhibitor or salts thereof further comprises **[L-NAME]** ***L^G-Nitro-L-arginine methyl ester hydrochloride***.

19. A method for the prophylaxis and treatment of rosacea and couperose which comprises applying to a patient in need thereof an effective amount of an NO-synthase inhibitor or salt thereof which is selected from the group consisting of **[L-MEA]** ***N^G-monoethyl-L-arginine monoacetate***, 2-Iminobiotin, **[L-NIO]** ***L-N^5-(1-iminoethyl)-ornithine***, S-Methylisothiourea sulphate, S-Methyl-L-thiocitrulline, **[L-NIL]** ***L-N^G-(1-iminoethyl)lysine***, 7-Nitroindazole, **[PBITU]** ***S,S'-1,3-Phenylene-bis(1,2-ethanediyl)-bis-isothiourea***, L-Thiocitrulline, **[alpha-N-acetyl-L-NAME]** ***alpha-N-acetyl-N^G-nitro-L-arginine methyl ester*** and salts thereof.

20. The method of claim 19, wherein said NO-synthase inhibitor is selected from the group consisting of 2-Iminobiotin, **[L-NIO]** ***L-N^5-(1-iminoethyl)-ornithine***, S-Methylisothiourea sulphate, S-Methyl-L-thiocitrulline, **[L-NIL]** ***L-N^G-(1-iminoethyl)lysine***, 7-Nitroindazole, **[PBITU]** ***S,S'-1,3-Phenylene-bis(1,2-ethanediyl)-bis-isothiourea***, L-Thiocitrulline, and salts thereof.

21. The method of claim 20, wherein said NO-synthase inhibitor or salt thereof further comprises **[L-NAME]** ***L^G-Nitro-L-arginine methyl ester hydrochloride***.

26. The preparation f claim 25, wherein the amount of NO-synthase inhibitor is from **[0.001% to 20%]** ***0.01% to 10%*** by weight based on the total weight of the preparation.

27. The preparation of claim 26, wherein the amount of NO-synthase inhibitor is from **[0.001% to 20%]** ***0.1% to 5%*** by weight based on the total weight of the preparation.